

### In the Claims

This listing of the claims will replace all prior versions, and listings, of claims in the application.

1.-29. (Cancelled)

30. (Currently Amended) A method of specifically cleaving a heparin-like glycosaminoglycan, comprising:

contacting a heparin-like glycosaminoglycan with the heparinase of any one of:

a substantially pure heparinase comprising a modified heparinase II having a modified product profile, wherein the modified product profile of the modified heparinase II is at least 10% different than a native product profile of a native heparinase II,

a substantially pure heparinase comprising a modified heparinase II that can cleave a glycosaminoglycan substrate having a modified heparinase II  $k_{cat}$  value, wherein the modified heparinase II  $k_{cat}$  value is at least 10% different than a native heparinase II  $k_{cat}$  value, and

a substantially pure heparinase comprising a modified heparinase I wherein the modified heparinase I has enzymatic activity that is not dependent on the presence of calcium,

wherein the modified heparinase II has the amino acid sequence of the mature peptide of SEQ ID NO: 2 or having conservative substitutions thereof, wherein ~~contains~~ at least one amino acid residue ~~that has been substituted with a different amino acid than in native heparinase II and wherein the residue that has been substituted~~ is selected from the group consisting of (a) a cysteine residue corresponding to position 348 ~~of SEQ ID NO: 2~~; (b) a histidine residue corresponding to at least one of positions 238, 252, 347, 440, 451, and 579 ~~of SEQ ID NO: 2~~; and (c) a heparin-binding sequence residue corresponding to at least one of positions 446-451 ~~of SEQ ID NO: 2~~, is substituted with a different amino acid than in native heparinase II.

and wherein the modified heparinase I has the amino acid sequence of the mature peptide of SEQ ID NO: 4 or having conservative substitutions thereof, wherein ~~contains~~ at least one amino acid residue ~~that has been substituted with a different amino acid than in native heparinase I, and wherein the residue that has been substituted~~ is a serine residue corresponding to position 377 ~~of SEQ ID NO: 4~~.

31. (Original) The method of claim 30, wherein the heparin-like glycosaminoglycan is contacted with a modified heparinase II, wherein the modified heparinase II has the amino acid sequence of the mature peptide of SEQ ID NO: 2 wherein the histidine residue corresponding to position 440 of SEQ. ID NO: 2 is substituted with a residue selected from the group consisting of alanine, serine, tyrosine, threonine, and lysine to specifically cleave a heparin-like glycosaminoglycan.

32. (Withdrawn) The method of claim 30, wherein the heparin-like glycosaminoglycan is contacted with a modified heparinase I, wherein the modified heparinase I has the amino acid sequence of the mature peptide of SEQ ID NO: 4 wherein at least one amino acid residue has been substituted and wherein the substitution is a substitution of a serine residue corresponding to position 377 of SEQ ID NO: 4 with a residue selected from the group consisting of alanine, serine, tyrosine, histidine, threonine, and lysine.

33. (Previously Presented) The method of claims 30, wherein the method is a method of removing heparin from a heparin containing fluid.

34. (Original) The method of claim 33, wherein the heparinase is immobilized on a solid support.

35.-45. (Cancelled)

46. (Currently Amended) A method of specifically cleaving a heparan sulfate-like glycosaminoglycan:

comprising contacting a heparan sulfate containing fluid with the heparinase of any one of:

a substantially pure heparinase comprising a modified heparinase II having a modified product profile, wherein the modified product profile of the modified heparinase II is at least 10% different than a native product profile of a native heparinase II and

a substantially pure heparinase comprising a modified heparinase II that can cleave a glycosaminoglycan substrate having a modified heparinase II  $k_{cat}$  value, wherein the modified heparinase II  $k_{cat}$  value is at least 10% different than a native heparinase II  $k_{cat}$  value.

wherein the modified heparinase II has the amino acid sequence of the mature peptide of SEQ ID NO: 2 or having conservative substitutions thereof, wherein ~~contains~~ at least one amino acid residue ~~that has been substituted with a different amino acid than in native heparinase II and wherein the residue that has been substituted~~ is selected from the group consisting of (a) a cysteine residue corresponding to position 348 ~~of SEQ ID NO: 2~~; (b) a histidine residue corresponding to at least one of positions 238, 252, 347, 440, 451, and 579 ~~of SEQ ID NO: 2~~; and (c) a heparin-binding sequence residue corresponding to at least one of positions 446-451 ~~of SEQ ID NO: 2~~, is substituted with a different amino acid than in native heparinase II.

47. (Previously Presented) The method of claim 46, wherein the method is a method of removing heparan sulfate from a heparan sulfate containing fluid.

48. (Original) The method of claim 47 wherein the heparinase is immobilized on a solid support.

49. (Original) The method of claim 46, wherein the heparan sulfate-like glycosaminoglycan is contacted with a substantially pure modified heparinase II, wherein the modified heparinase II has the amino acid sequence of the mature peptide of SEQ ID NO: 2 wherein the cysteine residue corresponding to position 348 of SEQ ID NO: 2 has been substituted with a residue selected from the group consisting of alanine, serine, tyrosine, histidine, threonine, and lysine to specifically cleave a heparin sulfate-like glycosaminoglycan.

50.-57. (Cancelled)